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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/772,675 | 02/04/2004 | George R. Krsek | KONEC 04.01 | 5597 |

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| EXAMINER | |
|---|---|
| DRODGE, JOSEPH W | |
| **ART UNIT** | **PAPER NUMBER** |
| 1723 | |

DATE MAILED: 05/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/772,675 | KRSEK ET AL. | |
| | Examiner | Art Unit | |
| | Joseph W. Drodge | 1723 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1-12 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-12 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 0604.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, also 6-9 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zavareh patent 6,121,453 in view of Harris et al patent 6,531,489, the internet publication "Organic Synthesis, Coll. Vol. 3, p. 544 (1955); Vol. 23, p.52 (1943), by Leffler et al, DBGET Factsheet for Compound C02344 and Bruson patent

1,920,160. Zavareh discloses isolating an d-threo-methylphenidate enantiomer or isomer of methylphenidate (an amine pharmaceutical) from the other 3 racemates/enantiomers/isomers (inherently comprising l-threo-methylphenidate of a mixture of which it is conventionally prepared (column 1, lines 10-15), by supplying an oxyacetic acid in the form of menthoxyacetic acid (column 1, lines 34-36), treating it with such chemical and collecting d-threo-menthylphenidate in at least 98% enatiomeric excess (column 2, lines 1-8).

The claims firstly all differ in requiring use of a different oxyacetic acid (fenchyloxyacetic acid). However, the factsheet and the Leffler et al article teach that fenchyloxyacetic acid and menthyoxyacetic acid have similar chemical structures and are similarly obtained from reactions of an alcohol and corresponding acetic acid monomer [as in instant claim 2], especially in combination with the Brunson patent (page 1, lines 49-63). Hence, it would have been obvious to one of ordinary skill in the art to have substituted one oxyacetic acid for another in the Zavareh process, as taught by Leffler et al, the factsheet and Brunson, since the chemicals are chemically similar and have similar chemical properties, selection of a particular oxyacetic acid being based on cost and availability {as suggested by Zavareh at column 1, lines 54-56 "...inexpensive...}.

The claims also differ in requiring achieving of 99% rather than 98% purity of the desired enantiomer. However, Harris et al achieves such purity of d-threo-methylphenidate, using treatment with another organic acid, by way of further purifying steps including filtering and washing with acetone (column 1, lines 60-68 and column 3,

lines 9-17). It would have been obvious to one of ordinary skill in the art to have augmented the Zavareh process with such further purifying steps to achieve at least 99% pure enantiomer, as taught by Harris et al, to achieve greater safety when administering the pharmaceutical drug to human patients {Harris at column 1, lines 60-61}.

Claim 6 and claims dependent therefrom also differ in requiring an additional step of treating the mixture to achieve an intermediate purity of at least 90% prior to the final treatment with oxyacetic acid that achieves 99% purity. Harris et al suggest such preliminary treatment step(s), both by reference to Patrick et al, supra at column 2, lines 19-22 and by suggestion of utilizing 2 stages or steps of dissolving the mixture in a solution of methanol and acetone, containing organic acid (see the Example, especially column 2, lines 60-64 combined with column 3, lines 9-17). It would have been further obvious to have added a further initial purifying step to the Zavareh process, as taught by Harris et al, to result in greater purity of the end product enantiomer.

Regarding claim 2, see Brunson at page 1, lines 53-63 and the Leffler publication regarding synthesis of oxyacetic acid.

For claims 3,7 and 9, salt cracking and chromatographic resolution steps are also disclosed by Zavareh at column 2,lines 33-34.

For claim 8, use of menthanolic solution, adding of water and filtering is taught by Harris et al at column 3, lines 13-14 and 22-27, and also suggested by Zavareh at column 2, lines 4-5.

Claims 4 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zavareh patent 6,121,453 in view of Harris et al patent 6,531,489, the internet publication "Organic Synthesis, Coll. Vol. 3, p. 544 (1955); Vol. 23, p.52 (1943), by Leffler et al, DBGET Factsheet for Compound C02344 and Bruson patent 1,920,160, as applied to claims 1-3 above, and further in view of Prashad et al patent 6,100,401. Claims 4 and 10 further differ in requiring treating the derived salt with an aqueous sodium bicarbonate solution and an acetate to give a 2-phase mixture and then treating the acetate fraction with hydrochloric acid. Harris et al teach use of aqueous sodium carbonate solution combined with treating with hydrochloric acid (column 2, lines 37-39 and column 3, lines 22-38) while Prashad teaches also use of acetate combined with later use of hydrochloric acid solution (column 3, lines 42-column 4, line 2). Zavareh suggests such prior art procedures being followed at column 1, last 2 lines-column 2, line 1 in the disclosure of "may be carried out...classical salt resolution procedures". It would have been further obvious to one of ordinary skill in the art to have utilized the treatment steps of Harris et al and Prashad et al in the salt resolution steps of Zavareh, since such procedures are known to result in a clean, robust separation of phases.

Claims 5 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zavareh patent 6,121,453 in view of Harris et al patent 6,531,489, the internet publication "Organic Synthesis, Coll. Vol. 3, p. 544 (1955); Vol. 23, p.52 (1943), by Leffler et al, DBGET Factsheet for Compound C02344 and Bruson patent 1,920,160, as well as Harris et al patent 6,531,489 applied to claim 4 above, and further in view of

Viterbo et al patent 3,848,030. For claims 5 and 11, Zavareh further discloses hydrolysis (hydrolyzing) followed by esterification to result in a ritalinic acid; the claims also require that the ritalinic acid be obtained by reaction with a menthanol solution saturated with hydrogen chloride. Viterbo et al teach such process step for purifying an isomer of methyphenidate (see column 3, lines 50-69 regarding methylphenidate, column 4, lines 70-75 regarding treatment with solutions comprising methanol, ethylacetate and HCL and column 5, lines 25-35 concerning rationale for forming optical isomers of acid form). It would have been additionally obvious to the skilled artisan to incorporate the specific steps of Viterbo et al in the forming of ritalinic acid disclosed by Zavareh, since such steps yield an acid form of the desired optical isomer which is stable and readily crystallizable to facilitate separation of the isomers.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Internet Supplied Publications by Prashad and Yakhontov et al are provided for general background regarding diverse methods of separating enantiomers of methylphenidate.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Drodge at telephone number 571-272-1140. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Wanda Walker, can reached at 571-272-1151. The fax phone number for the examining group where this application is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either private PAIR or Public PAIR, and through Private PAIR only for unpublished applications. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JWD

April 28, 2006

JOSEPH DRODGE
PRIMARY EXAMINER